Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp	
L1	7	"634740".ap.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:23	
L2	194	"fluorescent resonance energy transfer" and 435/6.ccls.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:26	
L3	134	"fluorescent resonance energy transfer" and 435/6.ccls. and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 16:51	
L4	130	"fluorescent resonance energy transfer" and 435/6.ccls. and covalent and modification	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:28	
L5	18	"fluorescent resonance energy transfer" and 435/6.ccls. and covalent and modification and histone	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:30	
L6	0	"fluorescent resonance energy transfer" and 435/6.ccls. and covalent and modification same histone	US-PGPUB; USPAT; EPO; DERWENT	OR	2005/07/26 15:30		
L7	0	"fluorescent resonance energy transfer" and 435/6.ccls. and covalent and histone same modification	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:31	
L8	0	"fluorescent resonance energy transfer" and 435/6.ccls. and histone same modification	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:31	
L9	0	"fluorescent resonance energy transfer" and histone same modification	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:32	
L10	49	"fluorescent resonance energy transfer" and histone and modification	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:32	
L11	7732	histone and modification	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:32	
L12	648	histone same modification	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:32	

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L13	33	histone same modification and FRET	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:33
L14	51	histone same modification and FRET or fluorescence with resonance with modification	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:35
L15	33	histone same modification and (FRET or fluorescence with resonance with modification)	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:35
L16	5	"634740".pn.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 16:50
L17	7	"634740".ap.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 16:50
L18	50	"fluorescent resonance energy transfer" and 435/7.1.ccls. and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 16:52
L19	0	"fluorescent resonance energy transfer" and 435/6.1.ccls. and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 16:52
L20	48	"fluorescent resonance energy transfer" and 435/69.1.ccls. and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 16:52
L21	0	"fluorescent resonance energy transfer" and 435/69.6.ccls. and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 16:52
L22	51	"fluorescent resonance energy transfer" and 435/320.1.ccls. and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 16:52
L23	1	"fluorescent resonance energy transfer" and 435/194.ccls. and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 16:53
L24	1	"fluorescent resonance energy transfer" and 530/358.ccls. and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 16:53

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S1	2	"6639063".pn.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/01/31 12:56
S2	5750	FRET	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/02/01 15:09
<b>S</b> 3	249	FRET and histone	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/02/01 15:09
S4	456	"fluorescent resonance energy transfer"	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:25
S5	47	"fluorescent resonance energy transfer" and histone	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/02/01 15:11
S6	0	"fluorescent resonance energy transfer" same histone	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/02/01 15:11
S7	0	"09865291".ap.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/02/02 09:53
S8	4	"865291".ap.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/02/02 09:53
S9	282	"I5" and histones	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/02/03 15:18

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\*ENCOMPPAT2 - EnCompass Patent File 1964-Present (Non-Supporters)

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F7	2	WPINDEX
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=> ("fluorescent resonance energy transfer" or FRET) and histone and modification 9 ("FLUORESCENT RESONANCE ENERGY TRANSFER" OR FRET) AND HISTONE AND MODIFICATION

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- ANSWER 1 OF 8 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on
- TI A fluorescence resonance energy transfer-based probe to monitor nucleosome structure
- ANSWER 2 OF 8 IFIPAT COPYRIGHT 2005 IFI on STN L4
- GENETICALLY ENCODED FLUORESCENT REPORTERS OF KINASE, METHYLTRANSFERASE, TI AND ACETYL-TRANSFERASE ACTIVITIES
- ANSWER 3 OF 8 IFIPAT COPYRIGHT 2005 IFI on STN L4
- CHEMICAL MODIFICATION OF DNA USING PEPTIDE NUCLEIC ACID TT CONJUGATES; PEPTIDE NUCLEIC ACIDS LINKED TO PEPTIDES WHICH HYBRIDIZE TO DNA AND CAN BE USED TO MONITOR THE INTRACELLULAR LOCATION OF EXOGENOUS TRANSFECTED DNA AND TO PROMOTE VARIOUS INTRACELLULAR PROCESSES
- L4 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Genetically encoded fusion protein fluorescent reporters of kinase, methyltransferase, and acetyltransferase activities in cells and tissues
- L4ANSWER 5 OF 8 Elsevier BIOBASE COPYRIGHT 2005 Elsevier Science B.V. on
- TI A genetically encoded fluorescent reporter of histone phosphorylation in living cells
- L4 ANSWER 6 OF 8 Elsevier BIOBASE COPYRIGHT 2005 Elsevier Science B.V. on
- TI Modulation of DNA conformations through the formation of alternative high-order HU-DNA complexes

- L4 ANSWER 7 OF 8 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 1
- TI Interaction of maize Opaque-2 and the transcriptional co-activators GCN5 and ADA2, in the modulation of transcriptional activity
- L4 ANSWER 8 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
- TI Selective recognition of acetylated **histones** by bromodomain proteins visualized in living cells.
- => d ab bib 1, 2, 4, 5, 8
- L4 ANSWER 1 OF 8 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
- Nucleosomes are the basic units of eukaryotic chromatin structure. AB restricting factor access to regulatory DNA sequences, nucleosomes significantly impact genomic processes such as transcription, and various mechanisms to alter nucleosome structure to relieve this repression have evolved. Both nucleosomes and processes that alter them are inherently dynamic in nature. Thus, studies of dynamics will be necessary to truly understand these relief mechanisms. We describe here the characteristics of a novel fluorescence resonance energy transfer-based reporter that can clearly signal the formation of a canonical nucleosome structure and follow conformational and compositional changes in that structure, both at the ensemble-average (bulk) and at the single molecule level. Labeled nucleosomes behave conformationally and thermodynamically like typical nucleosomes; thus they are relevant reporters of nucleosome behavior. Nucleosomes and free DNA are readily distinguishable at the single-molecule level. Thus, these labeled nucleosomes are well suited to studies of dynamic changes in nucleosome structure including single-molecule dynamics. © 2005 Elsevier Inc. All rights reserved.
- AN 2005:525011 SCISEARCH
- GA The Genuine Article (R) Number: 926KR
- TI A fluorescence resonance energy transfer-based probe to monitor nucleosome structure
- AU Lovullo D; Daniel D; Yodh J; Lohr D; Woodbury N W (Reprint)
- CS Arizona State Univ, Dept Chem & Biochem, Tempe, AZ 85287 USA (Reprint); Midwestern Univ, Coll Osteopath Med, Div Basic Sci, Glendale, AZ 85308 USA; Arizona State Univ, Biodesign Inst, Tempe, AZ 85287 USA nwoodbury@asu.edu
- CYA USA
- SO ANALYTICAL BIOCHEMISTRY, (1 JUN 2005) Vol. 341, No. 1, pp. 165-172. ISSN: 0003-2697.
- PB ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA.
- DT Article; Journal
- LA English
- REC Reference Count: 53
- ED Entered STN: 2 Jun 2005 Last Updated on STN: 2 Jun 2005
  - \*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*
- L4 ANSWER 2 OF 8 IFIPAT COPYRIGHT 2005 IFI on STN
- AB The invention provides fusion protein reporter molecules that can be used to monitor protein modifications (e.g., histone modifications) in living cells, and methods of using the fusion reporter molecules for diagnosing protein-modificationassociated disorders (e.g. histone-modification-associated disorders). The invention also provides methods of using the fusion protein reporters to identify candidate pharmaceutical agents that effect protein modification in cells and tissues, thus permitting identification of candidate pharmaceutical agents for treatment of protein-modification-associated disorders.

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ΑN
      10758652 IFIPAT; IFIUDB; IFICDB
      GENETICALLY ENCODED FLUORESCENT REPORTERS OF KINASE, METHYLTRANSFERASE,
TI
      AND ACETYL-TRANSFERASE ACTIVITIES
INF
      Ting; Alice Y., Cambridge, MA, US
      Ting Alice Y
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      Massachusetts Institute of Technology (52912)
PA
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      Avenue, Boston, MA, 02210, US
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      US 2004265906
                      A1 20041230
      US 2003-634740
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PRAI
      US 2002-425578P
                          20021112 (Provisional)
      US 2004265906
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DT
      Utility; Patent Application - First Publication
FS
      CHEMICAL
      APPLICATION
      This application claims priority under 35 U.S.C. (sec) 119 to U.S.
PARN
      provisional application Ser. No. 60/425,578, filed Nov. 12, 2002.
CLMN
      129
       7 Figure(s).
GI
     FIG. 1 is a diagram that shows the sites of post-translational
      modification on H3 and H4 tails. (=acetylation,
      upward-trinaglefilled =methylation, and *=phosphorylation. (Adapted from
      Zhang, Y. and Reinberg, D. Genes and Dev. 15:2343-2360, (2001)).
     FIG. 2 shows a schematic design of a fusion protein reporter. FIG. 2A
      shows a general design of a FRET-based indicator of
      histone modification state in living cells. The
      modificationspecific binding domain may be a 14-3-3 or FHA domain for
      detecting histone phosphorylation, a bromodomain for detecting
      acetylation, or a chromodomain for detecting methylation. FIG. 2B shows
      the domain structure of an indicator for detecting acetyltransferase
      activity. The bromodomain comes from one of several bromodomain-
      containing proteins. The substrate consists of either the H3 or H4
      N-terminal peptide. The acetylationcompetent lysines are underlined. The
      entire reporter can be fused to localization signals or specialized
      proteins for targeting to specific enzymes, DNA sequences, or chromatin
      regions. ARTKQTARKSTGGKAPRKQLATKAARKSAPATGGVKKPHR is an H3 Nterminal
      peptide (SEQ ID NO:1) and SGRGKGGKGLGKGGAKRHRKVLRDNIQGIT is an H4
      N-terminal peptide (SEQ ID NO:2).
     FIG. 3 shows diagrams of fusion protein reporter constructs that have been
      produced. FIG. 3A shows histone acetyltansferase indicator
      fusion protein reporters and FIG. 3B shows kinase indicator fusion
      protein reporters.
     FIG. 4 shows a diagram of the domain structure of the histone 3
      phosphorylation indicator (FIG. 4A). The H3 peptide segment
      (ARTKQTARKSTGGKAPRKQLATKAARKSAP; SEQ ID NO: 18) of the indicator
      corresponds to the first 30 amino acids of the H3 protein. The known
      phosphorylation sites (S10 and 28) are underlined. FIG. 4B is a digitized
      image of Western blots depicting the phosphorylation state of the
      original reporter and the four point mutants after 600-minute reactions
      with Msk1 and ATP at 30 degrees C. As expected, the original reporter and
      the K49E mutant have phosphate groups at both the S10 and S28 sites,
      while the other mutants lack one or both of the phosphate marks.
     FIG. 5 is a histogram showing the distribution of YFP/CFP emission ratios
      for 71 nocodazole-treated cells and 131 untreated cells.
      Nocodazole-treated cells display, on average, higher emission ratios than
      untreated cells, consistent with increased H3-S28 phosphorylation levels.
      The experimental mean difference is 0.05, outside the 95% confidence
      interval for a distribution with standard deviation of 0.0511.
     FIG. 6 is a diagram of the domain structure of the H4 acetylation
      indicator. The H4 peptide shown is SGRGKGGKGLGKGGAKRHRKVLRDNIQGIT (SEQ ID
      NO:2).
```

FIG. 7 shows a diagram of the domain structure of the H3 methylation

indicator (FIG. 7A; ARTKQTARKSTGGKAPRKQLATKAARKSAP (SEQ ID NO:18)). The lysine in H3 recognized by the HP 1 chromodomain is underlined. FIG. 7B is a digitized image of an immunoblot with alpha-methyl-H3-K9 antibody showing reporter methylation after 6 hours at 30 degrees C. under the same reaction conditions: 3.5 mu M reporter, 50 mM Tris pH 8.5, 20 mM KCl, 10 mM MgCl2, 2 mM S-adenosylmethionine (SAM), 1.7 mM DTT, and an undetermined concentration of GST-tagged G9a). With either SAM or G9a left out, no methylation was observed.

- L4 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
- The invention provides fusion protein reporter mols. that can be used to AB monitor protein modifications (e.g., histone modifications) in living cells, and methods of using the fusion reporter mols. for diagnosing protein-modification-associated disorders (e.g. histone-modification-associated disorders). Reporters are designed by fusing, in order from N- to C-terminus, cyan fluorescent protein (CFP), a binding domain specific for the modified histone sequence of interest, a peptide substrate corresponding to the N-terminus of histone H3 or H4, and yellow fluorescent protein (YFP). Modification of the peptide substrate by a kinase, acetyltransferase, or methyltransferase then allows it to form an intramol. complex with the binding domain, increasing fluorescence resonance energy transfer (FRET) between the two flanking fluorescent moieties. Removal of the modification by a phosphatase, deacetylase, or (if methylation is reversible) demethylase reverses the FRET change. This design is optimized empirically to maximize responsivity by interchanging the donor and acceptor or the substrate and binding domain, or by varying the length and content of interdomain spacer sequences (linker sequences). Gcn5-based and TAFAB-based histone acetylation reporters are emphasized. The invention also provides methods of using the fusion protein reporters to identify candidate pharmaceutical agents that effect protein modification in cells and tissues, thus permitting identification of candidate pharmaceutical agents for treatment of proteinmodification-associated disorders.
- AN 2004:430935 CAPLUS
- DN 141:18691
- TI Genetically encoded fusion protein fluorescent reporters of kinase, methyltransferase, and acetyltransferase activities in cells and tissues
- IN Ting, Alice Y.
- PA Massachusetts Institute of Technology, USA
- SO PCT Int. Appl., 96 pp.
- CODEN: PIXXD2
  DT Patent
- LA English
- FAN.CNT 1

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PRAI		2002 2003				P A		2002	1112 0805									

- L4 ANSWER 5 OF 8 Elsevier BIOBASE COPYRIGHT 2005 Elsevier Science B.V. on STN
- AB An increase in FRET indicates phosphorylation of histone H3 at serine 28. The protein-based reporter (see picture) responds to phosphorylation through intramolecular complexation between a substrate domain derived from histone H3 and a linked

phosphoserine-recognition domain. The reporter is also effective inside living mammalian cells. **FRET** = fluorescence resonance energy transfer.

AN 2004244172 ESBIOBASE

TI A genetically encoded fluorescent reporter of **histone** phosphorylation in living cells

AU Lin C.-W.; Ting A.Y.

CS Prof. A.Y. Ting, Department of Chemistry, Massachusetts Inst. of Technology, Cambridge, MA 02139, United States. E-mail: ating@mit.edu

SO Angewandte Chemie - International Edition, (24 MAY 2004), 43/22 (2940-2943), 15 reference(s)
CODEN: ACIEAY ISSN: 1433-7851

DT Journal; Article

CY Germany, Federal Republic of

LA English

SL English

AB

L4 ANSWER 8 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

Acetylation and other modifications on histones comprise histone codes that govern transcriptional regulatory processes in chromatin. Yet little is known how different histone codes are translated and put into action. Using fluorescence resonance energy transfer, we show that bromodomain-containing proteins recognize different patterns of acetylated histones in intact nuclei of living cells. The bromodomain protein Brd2 selectively interacted with acetylated lysine 12 on histone H4, whereas TAFdblvert250 and PCAF recognized H3 and other acetylated histones, indicating fine specificity of histone recognition by different bromodomains. This hierarchy of interactions was also seen in direct peptide binding assays. Interaction with acetylated histone was essential for Brd2 to amplify transcription. Moreover association of Brd2, but not other bromodomain proteins, with acetylated chromatin persisted on chromosomes during mitosis. Thus the recognition of histone acetylation code by bromodomains is selective, is involved in transcription, and potentially conveys transcriptional memory across cell divisions.

AN 2004:149090 BIOSIS

DN PREV200400152814

TI Selective recognition of acetylated **histones** by bromodomain proteins visualized in living cells.

AU Kanno, Tomohiko; Kanno, Yuka; Siegel, Richard M.; Jang, Moon Kyoo; Lenardo, Michael J.; Ozato, Keiko [Reprint Author]

CS Laboratory of Molecular Growth Regulation, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, 20892, USA ozatok@nih.gov

SO Molecular Cell, (January 16 2004) Vol. 13, No. 1, pp. 33-43. print. ISSN: 1097-2765 (ISSN print).

DT Article

LA English

ED Entered STN: 17 Mar 2004

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